

B-11

[illegible]

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B-20

Talc, NTP TR 421

TABLE B2

Individual Animal Tumor Pathology of Female Rats in the Lifetime Inhalation Study of Talc: 18 mg/m³ (continued)

Number of Days on Study	5 5 5 5 6 6 6 6 6 6 6 6 6 6 6 7 7 7 7 7 7 7 7 7
	3 5 8 9 1 3 4 6 6 7 7 7 8 9 9 0 1 1 1 2 3 4 4 4 7
	6 8 6 4 5 3 6 0 1 5 6 8 4 3 7 6 0 6 7 4 9 0 6 7 3
Carcass ID Number	1 2 2 2 1 2 2 2 1 2 2 2 2 2 1 2 1 2 2 2 1 2 1 2 2
	6 8 1 1 8 8 3 8 8 8 0 5 0 4 8 0 6 8 3 5 8 6 9 3 0
	7 0 6 2 3 5 0 1 6 8 7 5 8 0 9 6 0 2 6 6 1 3 2 9 9
	1 1
Endocrine System (continued)	
Pituitary gland	+ +
Pars distalis, adenoma	X X X X X
Pars distalis, carcinoma	X
Thyroid gland	+ + A +
C-cell, adenoma	X X
C-cell, carcinoma	X X
General Body System	
None	
Genital System	
Clitoral gland	+ M + M +
Adenoma	
Carcinoma	
Ovary	+ +
Bilateral, granulosa-theca tumor	
malignant	X
Uterus	+ +
Polyp stromal	X
Hematopoietic System	
Bone marrow	+ + A +
Lymph node	+ +
Lymph node, bronchial	+ + + + + + + + + + + M + + M + + + + M + + + +
Squamous cell carcinoma, metastatic, lung	X
Lymph node, mandibular	+ + + + + + + M + + + + + + + + + + + + + + M + +
Lymph node, mediastinal	+ +
Carcinoma, metastatic, uncertain primary site	
Fibrosarcoma, metastatic, skin	X
Granulosa-theca tumor malignant, metastatic, ovary	X
Lymph node, mesenteric	+ + A +
Spleen	+ +
Thymus	+ + + M M + + + + + + + + + + + + + + + + + +
Schwannoma benign	

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B-22

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TABLE B2

Individual Animal Tumor Pathology of Female Rats in the Lifetime Inhalation Study of Talc: 18 mg/m³ (continued)

Number of Days on Study	5 5 5 5 6 6 6 6 6 6 6 6 6 6 6 7 7 7 7 7 7 7 7 7 7
	3 5 8 9 1 3 4 6 6 7 7 7 8 9 9 0 1 1 1 2 3 4 4 4 7
	6 8 6 4 5 3 6 0 1 5 6 8 4 3 7 6 0 6 7 4 9 0 6 7 3
Carcass ID Number	1 2 2 2 1 2 2 2 1 2 2 2 2 2 1 2 1 2 2 2 1 2 1 2 2
	6 8 1 1 8 8 3 8 8 8 0 5 0 4 8 0 6 8 3 5 8 6 9 3 0
	7 0 6 2 3 5 0 1 6 8 7 5 8 0 9 6 0 2 6 6 1 3 2 9 9
	1 1
Integumentary System	
Mammary gland	+ +
Adenocarcinoma	
Adenoma	
Fibroadenoma	
Fibrosarcoma	X X X X X
Skin	+ +
Keratoacanthoma	X
Subcutaneous tissue, fibrosarcoma	X
Musculoskeletal System	
Bone	+ +
Nervous System	
Brain	+ +
Carcinoma, metastatic, pituitary gland	X
Respiratory System	
Larynx	+ + + + + I + I + + + + + + + + + + + + + + + +
Lung	+ +
Alveolar/bronchiolar adenoma	
Alveolar/bronchiolar adenoma, multiple	X X
Alveolar/bronchiolar carcinoma	
Alveolar/bronchiolar carcinoma, multiple	
Granulosa-theca tumor malignant, metastatic, ovary	X
Squamous cell carcinoma	X
Nose	+ + + + + + + + + + + + + + + A + + + + + + + +
Trachea	+ +
Special Senses System	
Eye	
Harderian gland	+ +
Lacrimal gland	
Urinary System	
Kidney	+ + A +
Urinary bladder	+ +
Systemic Lesions	
Multiple organs	+ +
Leukemia mononuclear	X X X X X X X X X X X X X X X X X X

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B-24

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TABLE B3

Statistical Analysis of Primary Neoplasms in Female Rats in the Lifetime Inhalation Study of Talc

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Adrenal Medulla: Benign Pheochromocytoma			
Overall rates ^a	13/48 (27%)	14/47 (30%)	18/49 (37%)
Adjusted rates ^b	61.3%	59.7%	82.5%
Terminal rates ^c	5/11 (45%)	5/13 (38%)	6/9 (67%)
First incidence (days)	678	705	697
Life table tests ^d	P=0.135	P=0.529	P=0.183
Logistic regression tests ^d	P=0.185	P=0.541	P=0.225
Cochran-Armitage test ^d	P=0.180		
Fisher exact test ^e		P=0.474	P=0.212
Adrenal Medulla: Malignant Pheochromocytoma			
Overall rates	0/48 (0%)	1/47 (2%)	10/49 (20%)
Adjusted rates	0.0%	7.1%	56.9%
Terminal rates	0/11 (0%)	0/13 (0%)	3/9 (33%)
First incidence (days)	— ^e	849	784
Life table tests	P<0.001	P=0.531	P=0.002
Logistic regression tests	P<0.001	P=0.509	P=0.001
Cochran-Armitage test	P<0.001		
Fisher exact test		P=0.495	P<0.001
Adrenal Medulla: Benign or Malignant Pheochromocytoma			
Overall rates	13/48 (27%)	14/47 (30%)	23/49 (47%)
Adjusted rates	61.3%	59.7%	95.2%
Terminal rates	5/11 (45%)	5/13 (38%)	8/9 (89%)
First incidence (days)	678	705	697
Life table tests	P=0.016	P=0.529	P=0.033
Logistic regression tests	P=0.014	P=0.541	P=0.024
Cochran-Armitage test	P=0.021		
Fisher exact test		P=0.474	P=0.034
Liver: Neoplastic Nodule			
Overall rates	0/50 (0%)	3/48 (6%)	1/50 (2%)
Adjusted rates	0.0%	13.6%	10.0%
Terminal rates	0/11 (0%)	0/13 (0%)	0/9 (0%)
First incidence (days)	—	724	857
Life table tests	P=0.550	P=0.114	P=0.464
Logistic regression tests	P=0.561	P=0.117	P=0.496
Cochran-Armitage test	P=0.556		
Fisher exact test		P=0.114	P=0.500
Liver: Neoplastic Nodule or Hepatocellular Carcinoma			
Overall rates	0/50 (0%)	4/48 (8%)	1/50 (2%)
Adjusted rates	0.0%	20.2%	10.0%
Terminal rates	0/11 (0%)	1/13 (8%)	0/9 (0%)
First incidence (days)	—	724	857
Life table tests	P=0.575	P=0.066	P=0.464
Logistic regression tests	P=0.602	P=0.060	P=0.496
Cochran-Armitage test	P=0.599		
Fisher exact test		P=0.054	P=0.500

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Lesions in Female Rats

B-25

TABLE B3

Statistical Analysis of Primary Neoplasms in Female Rats in the Lifetime Inhalation Study of Talc (continued)

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Lung: Alveolar/bronchiolar Adenoma			
Overall rates	1/50 (2%)	0/48 (0%)	9/50 (18%)
Adjusted rates	4.5%	0.0%	40.8%
Terminal rates	0/11 (0%)	0/13 (0%)	1/9 (11%)
First incidence (days)	805	-	716
Life table tests	P<0.001	P=0.529N	P=0.015
Logistic regression tests	P<0.001	P=0.503N	P=0.010
Cochran-Armitage test	P<0.001		
Fisher exact test		P=0.510N	P=0.008
Lung: Alveolar/bronchiolar Carcinoma			
Overall rates	0/50 (0%)	0/48 (0%)	5/50 (10%)
Adjusted rates	0.0%	0.0%	41.7%
Terminal rates	0/11 (0%)	0/13 (0%)	3/9 (33%)
First incidence (days)	-	-	828
Life table tests	P=0.002	-	P=0.027
Logistic regression tests	P=0.003	-	P=0.028
Cochran-Armitage test	P=0.004		
Fisher exact test		-	P=0.028
Lung: Alveolar/bronchiolar Adenoma or Carcinoma			
Overall rates	1/50 (2%)	0/48 (0%)	13/50 (26%)
Adjusted rates	4.5%	0.0%	65.8%
Terminal rates	0/11 (0%)	0/13 (0%)	4/9 (44%)
First incidence (days)	805	-	716
Life table tests	P<0.001	P=0.529N	P=0.001
Logistic regression tests	P<0.001	P=0.503N	P<0.001
Cochran-Armitage test	P<0.001		
Fisher exact test		P=0.510N	P<0.001
Mammary Gland: Fibroadenoma			
Overall rates	11/50 (22%)	10/49 (20%)	13/50 (26%)
Adjusted rates	47.6%	41.4%	64.0%
Terminal rates	2/11 (18%)	3/13 (23%)	4/9 (44%)
First incidence (days)	634	482	678
Life table tests	P=0.304	P=0.489N	P=0.394
Logistic regression tests	P=0.363	P=0.508N	P=0.428
Cochran-Armitage test	P=0.343		
Fisher exact test		P=0.521N	P=0.408
Mammary Gland: Fibroma, Fibroadenoma, or Adenoma			
Overall rates	13/50 (26%)	13/49 (27%)	15/50 (30%)
Adjusted rates	54.7%	59.0%	68.6%
Terminal rates	3/11 (27%)	6/13 (46%)	4/9 (44%)
First incidence (days)	634	482	678
Life table tests	P=0.314	P=0.544N	P=0.404
Logistic regression tests	P=0.394	P=0.585	P=0.434
Cochran-Armitage test	P=0.371		
Fisher exact test		P=0.567	P=0.412

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B-26

Talc, NTP TR 421

TABLE B3

Statistical Analysis of Primary Neoplasms in Female Rats in the Lifetime Inhalation Study of Talc (continued)

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Mammary Gland: Fibroma, Fibroadenoma, Adenoma, or Adenocarcinoma			
Overall rates	15/50 (30%)	13/49 (27%)	16/50 (32%)
Adjusted rates	56.6%	59.0%	70.1%
Terminal rates	3/11 (27%)	6/13 (46%)	4/9 (44%)
First incidence (days)	370	482	678
Life table tests	P=0.378	P=0.386N	P=0.494
Logistic regression tests	P=0.457	P=0.425N	P=0.531
Cochran-Armitage test	P=0.430		
Fisher exact test		P=0.437N	P=0.500
Pituitary Gland (Pars Distalis): Adenoma			
Overall rates	19/50 (38%)	18/47 (38%)	21/50 (42%)
Adjusted rates	62.1%	60.5%	78.3%
Terminal rates	3/11 (27%)	3/13 (23%)	4/9 (44%)
First incidence (days)	568	697	633
Life table tests	P=0.360	P=0.512N	P=0.425
Logistic regression tests	P=0.409	P=0.557N	P=0.457
Cochran-Armitage test	P=0.380		
Fisher exact test		P=0.571	P=0.419
Pituitary Gland (Pars Distalis): Carcinoma			
Overall rates	3/50 (6%)	3/47 (6%)	2/50 (4%)
Adjusted rates	17.1%	12.2%	5.6%
Terminal rates	1/11 (9%)	1/13 (8%)	0/9 (0%)
First incidence (days)	696	566	676
Life table tests	P=0.438N	P=0.636N	P=0.506N
Logistic regression tests	P=0.427N	P=0.634	P=0.497N
Cochran-Armitage test	P=0.418N		
Fisher exact test		P=0.631	P=0.500N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma			
Overall rates	22/50 (44%)	21/47 (45%)	23/50 (46%)
Adjusted rates	69.8%	66.2%	79.5%
Terminal rates	4/11 (36%)	4/13 (31%)	4/9 (44%)
First incidence (days)	568	566	633
Life table tests	P=0.429	P=0.502N	P=0.488
Logistic regression tests	P=0.506	P=0.570N	P=0.545
Cochran-Armitage test	P=0.471		
Fisher exact test		P=0.554	P=0.500
Thyroid Gland (C-cell): Adenoma			
Overall rates	5/50 (10%)	0/47 (0%)	6/49 (12%)
Adjusted rates	33.5%	0.0%	34.0%
Terminal rates	2/11 (18%)	0/13 (0%)	2/9 (22%)
First incidence (days)	805	-	678
Life table tests	P=0.253	P=0.030N	P=0.467
Logistic regression tests	P=0.283	P=0.029N	P=0.505
Cochran-Armitage test	P=0.276		
Fisher exact test		P=0.033N	P=0.486

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Lesions in Female Rats

B-27

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the Lifetime Inhalation Study of Talc (continued)

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Thyroid Gland (C-cell): Carcinoma			
Overall rates	3/50 (6%)	2/47 (4%)	2/49 (4%)
Adjusted rates	11.1%	12.2%	4.9%
Terminal rates	0/11 (0%)	0/13 (0%)	0/9 (0%)
First incidence (days)	677	818	675
Life table tests	P=0.430N	P=0.507N	P=0.493N
Logistic regression tests	P=0.462N	P=0.516N	P=0.533N
Cochran-Armitage test	P=0.463N		
Fisher exact test		P=0.530N	P=0.510N
Thyroid Gland (C-cell): Adenoma or Carcinoma			
Overall rates	8/50 (16%)	2/47 (4%)	8/49 (16%)
Adjusted rates	40.9%	12.2%	37.2%
Terminal rates	2/11 (18%)	0/13 (0%)	2/9 (22%)
First incidence (days)	677	818	675
Life table tests	P=0.418	P=0.051N	P=0.579
Logistic regression tests	P=0.435	P=0.048N	P=0.599N
Cochran-Armitage test	P=0.414		
Fisher exact test		P=0.056N	P=0.590
Uterus: Stromal Polyp			
Overall rates	5/50 (10%)	7/49 (14%)	4/50 (8%)
Adjusted rates	22.3%	34.4%	19.5%
Terminal rates	1/11 (9%)	3/13 (23%)	1/9 (11%)
First incidence (days)	398	678	678
Life table tests	P=0.439N	P=0.400	P=0.532N
Logistic regression tests	P=0.376N	P=0.372	P=0.505N
Cochran-Armitage test	P=0.386N		
Fisher exact test		P=0.365	P=0.500N
Uterus: Stromal Polyp or Stromal Sarcoma			
Overall rates	5/50 (10%)	8/49 (16%)	4/50 (8%)
Adjusted rates	22.3%	35.8%	19.5%
Terminal rates	1/11 (9%)	3/13 (23%)	1/9 (11%)
First incidence (days)	398	557	678
Life table tests	P=0.412N	P=0.298	P=0.532N
Logistic regression tests	P=0.360N	P=0.265	P=0.505N
Cochran-Armitage test	P=0.363N		
Fisher exact test		P=0.264	P=0.500N
All Organs: Mononuclear Cell Leukemia			
Overall rates	13/50 (26%)	20/49 (41%)	18/50 (36%)
Adjusted rates	45.7%	73.3%	60.1%
Terminal rates	1/11 (9%)	8/13 (62%)	3/9 (33%)
First incidence (days)	390	526	536
Life table tests	P=0.234	P=0.164	P=0.232
Logistic regression tests	P=0.226	P=0.084	P=0.152
Cochran-Armitage test	P=0.250		
Fisher exact test		P=0.088	P=0.194

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B-28

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TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the Lifetime Inhalation Study of Talc (continued)

	0 mg/m ³	6 mg/m ³	18 mg/m ³
All Organs: Malignant Lymphoma			
Overall rates	0/50 (0%)	3/49 (6%)	0/50 (0%)
Adjusted rates	0.0%	10.3%	0.0%
Terminal rates	0/11 (0%)	0/13 (0%)	0/9 (0%)
First incidence (days)	-	724	-
Life table tests	P=0.525N	P=0.124	-
Logistic regression tests	P=0.497N	P=0.118	-
Cochran-Armitage test	P=0.499N		
Fisher exact test		P=0.117	-
All Organs: Benign Tumors			
Overall rates	38/50 (76%)	35/49 (71%)	39/50 (78%)
Adjusted rates	97.2%	96.9%	97.4%
Terminal rates	10/11 (91%)	12/13 (92%)	8/9 (89%)
First incidence (days)	398	482	558
Life table tests	P=0.338	P=0.350N	P=0.440
Logistic regression tests	P=0.544	P=0.312N	P=0.562N
Cochran-Armitage test	P=0.415		
Fisher exact test		P=0.387N	P=0.500
All Organs: Malignant Tumors			
Overall rates	23/50 (46%)	31/49 (63%)	35/50 (70%)
Adjusted rates	69.3%	85.8%	90.5%
Terminal rates	4/11 (36%)	9/13 (69%)	6/9 (67%)
First incidence (days)	370	526	536
Life table tests	P=0.054	P=0.189	P=0.061
Logistic regression tests	P=0.013	P=0.056	P=0.010
Cochran-Armitage test	P=0.016		
Fisher exact test		P=0.064	P=0.013
All Organs: Benign or Malignant Tumors			
Overall rates	44/50 (88%)	47/49 (96%)	49/50 (98%)
Adjusted rates	97.6%	97.9%	100.0%
Terminal rates	10/11 (91%)	12/13 (92%)	9/9 (100%)
First incidence (days)	370	482	536
Life table tests	P=0.248	P=0.447	P=0.279
Logistic regression tests	P=0.053	P=0.145	P=0.060
Cochran-Armitage test	P=0.049		
Fisher exact test		P=0.141	P=0.056

^a Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.

^b Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality

^c Observed incidence at terminal kill

^d Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.

^e Not applicable; no tumors in animal group

^f Value of statistic cannot be computed.

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